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ABSTRACTS

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## CLINICAL STUDIES, TUBERCULOSIS

**Trends in Treatment.**—Trends in the treatment of tuberculosis are demonstrated by comparing 1948 admissions to a large suburban sanatorium with those in 1953. Although the rate of admission had increased 20 per cent, the number discharging tubercles in their sputum had markedly decreased. This is ascribed to a higher percentage of early cases and the fact that a large proportion had received antibiotics before admission in 1953. Pneumothorax is still the favorite means of collapse therapy, but its use has decreased in the five years while forms of surgical collapse have increased. There were no cases of pneumoperitoneum in 1948 and 4 in 1953. Surgical excision is still rare.—*L'évolution des traitements de la tuberculose pulmonaire commune d'après les entrées en sanatorium, J. Bernheim, Poumon, April, 1953, 9: 249.*—(*F. S. Lansdown*)

**Tertiary Tuberculosis.**—Many cases of "tertiary" tuberculosis have been observed in a sanatorium with symptoms varying from the systemic debility or lack of energy described by Burnard to the grippe-like illness of Landuzy's "typhobacillose". The prolonged impact of imperfectly cured tuberculosis produces various pathologic changes. These may be caused directly by the spread of supposedly arrested lesions, the conveyance of infection by the blood or lymph channels, or by lessened tissue resistance due to toxins. Such lesions occur particularly in old people with smoldering, fairly well-tolerated foci but are also found in younger patients. This is especially true of those who have small chronic cavities which have been reduced in size by the sanatorium regimen, antibiotics, chemotherapy, and collapse therapy. Most chronic cavities are less than 2.5 cm. in diameter. Twenty-five years ago, such lesions spread rapidly and the patient died while still in the sanatorium. Nowadays, this may occur long after his first discharge. In 1951, only 40 per cent of 200 patients had cavities and, of these, only 8 per cent died or left the sanatorium infectious. In spite of encystment with the formation of a collagen and fibrous tissue walls, new pathologic changes finally occur, sometimes in remote areas, as alveolar inflammations of different types, pneumonic areas, fatty changes, or caseous alterations. In 3 illustrative cases, chronic cavities were well tolerated for a time but were eventually followed by serious lesions in the esophagus. In one case a fatal fistula developed between the cavity and the esophagus. In another case, bronchopneumonia had occurred with involvement of the axillary and cervical glands. Eighteen years after oleothorax had been used with favorable effects, the patient developed difficulty in swallowing from stenosis of the larynx due to external pressure of enlarged glands. In the third case, seven years after pneumothorax followed by paraffin and gomenol filling of the pleural cavity, there was functional difficulty in swallowing. This was caused by the pressure of oil which had leaked from the pleural cavity into the mediastinal tissues. Surgical attempts to relieve the situation failed, and the patient died.—*A propos de la pathologie oesophagienne au cours de la tuberculose pulmonaire, P. Toussaint, Acta tuberc. belg., April, 1953, 44: 302.*—(*A. T. Laird*)

**Treatment by Pleural Irritation.**—A persistent cavity in a lung may close when exuda-

tive pleurisy develops. This observation led to attempts to produce pleurisy. Intrapleural instillation of 1 gm. of streptomycin in 2 cc. of saline twice a week has proved effective in cases of ineffective pneumothorax. It is believed that a reflectory contraction of bronchi and bronchioles causes atelectasis and cavity closure.—*Zur Pleurareiztherapie, R. Graf, Wien. klin. Wchnschr., August 7, 1953, 65: 644.*—(*G. C. Leiner*)

**Atypical Tuberculin Reactions.**—In 6 cases of active tuberculosis, atypical tuberculin reactions were noted, consisting of the appearance of a large area of marked erythema and a small area of infiltration at twenty-four hours and their complete waning at forty-eight hours, usually following a large dose of intracutaneously administered tuberculin. These, as a rule, are false positive reactions but may rarely occur during certain phases of active tuberculosis. Therefore, if this type of reaction is encountered in a case of pulmonary lesion of undetermined nature, it should not be interpreted as definite evidence against the diagnosis of active pulmonary tuberculosis (Author's summary).—*Atypical tuberculin reactions, L. S. Arany, J.A.M.A., June 6, 1953, 152: 491.*—(*H. Abeles*)

**Pure Oxygen in Tuberculosis.**—The breathing of anoxic mixtures causes an increase in pulmonary arterial pressure which is attributed to a local action on the blood vessel walls. This results in constriction of the pulmonary arterioles and an increase in pulmonary arterial pressures. Euler and Lilejstrand found that breathing pure oxygen caused a fall in pulmonary arterial pressure of cats which they believed was the result of dilatation of the pulmonary vasculature. In this study the effect of breathing 100 per cent oxygen was determined in 27 patients with advanced pulmonary tuberculosis and 25 patients with mitral stenosis. In each group 22 and 21 patients, respectively, showed a statistically significant decrease in pulmonary artery pressure. There was a definite correlation between the control mean pulmonary arterial pressure and the degree of its decrease. It seemed to the authors that the decrease probably was not primarily due to a reduction in the volume of blood flowing through the pulmonary vascular bed. They believed that a fall in left atrial and pulmonary venous pressure might account for the decrease in mitral stenosis but not in pulmonary tuberculosis. It did seem possible that this could be due to a decrease in pulmonary vascular resistance. Whatever the cause, it has been demonstrated that the beneficial effect of oxygen therapy in patients with acute or chronic pulmonary arterial hypertension may depend, not only upon the factors of increased arterial oxygen tension, decreased cardiac output, and decreased cardiac rate, but also upon a decreased pulmonary arterial pressure, a factor which would further reduce the work of the right ventricle. —*The effect of breathing 100 per cent oxygen on the pulmonary arterial pressure in patients with pulmonary tuberculosis and mitral stenosis, S. H. Dressler, N. B. Slonim, O. J. Balchum, G. J. Bronfin, & A. Ravin, J. Clin. Investigation, September, 1952, 31: 807.*—(*S. J. Hadley*)

## CLINICAL STUDIES, NONTUBERCULOUS DISEASES

**Smoker's Respiratory Syndrome.**—A clinical syndrome characterized by dyspnea wheezing, constriction in the throat and upper air passages, and pain in the chest associated with a tendency to frequent upper respiratory infections occurs in smokers. The most constant clinical feature is chronic pharyngitis. The chest roentgenogram usually reveals accentuated hilar markings. There is usually no allergic background and no eosinophilia in the blood or in the nasal and bronchial secretions. Skin reactions to tobacco smoke or tobacco extract are normal. Exposure to such irritants as odors of paints, burning wood, frying fat, and grain dust may bring about asthma-like wheezing. The paroxysms of wheezing are not nearly as distressing as those of allergic asthma. The wheezing is localized principally in the tracheobronchial region. This syndrome was observed in 31

patients. It is induced by smoking and subsides on elimination of smoking.—*Smoker's respiratory syndrome, a clinical entity, G. L. Waldbott, J.A.M.A., April 18, 1953, 151: 1398.*—(*H. Abeles*)

**Bronchiectasis.**—A survey upon a population of nearly 150,000 lasting for five years disclosed 166 patients with bronchiectasis confirmed by bronchograms; a further 48 had undoubted bronchiectasis, but in the absence of confirmatory bronchograms they were ignored in the analysis. Bronchiectasis was present in at least 1.3 per thousand. The distribution and type of bronchiectasis found were not greatly different from those previously reported, but an usually large number of cases were due to primary tuberculosis and mustard gas. The symptoms were less severe and universal than those reported in most general series and approached those found in selected groups considered fit for military service. Only 5 patients less than 60 years of age were unable to work. In only 3 patients were postero-anterior roentgenograms normal. Comparisons between cases diagnosed in teaching or large hospitals and the remainder show that those diagnosed in such hospitals had more extensive disease and severe symptoms. Those patients with disease of less than lobar extent had, on the contrary, fewer symptoms than the rest. The period under observation averaged three years, during which time there were 6 deaths, all in bilateral cases or from complications not due to bronchiectasis. There were no deaths from pneumonia or other pyogenic complications. The condition of the remainder changed little. The treatment was mainly medical, but 6 patients were treated by resection. There are reasons for postulating that the prognosis of the medically treated patient is not so bad as has been stated previously and that this is largely due to the advent of chemotherapy. It may not be justifiable to advocate surgery whenever this is possible; a high proportion of bronchiectatic persons remain well and are little inconvenienced by their disease if competently treated by postural drainage and antibiotics. The latter statement applies particularly to the operable group (Author's summary).—*Bronchiectasis: A study centered on Bedford and its environs, N. Wynn-Williams, Brit. M. J., May 30, 1953, No. 4821: 1194.*—(*E. A. Riley*)

**Pulmonary Paragonimiasis.**—Hemoptysis in any patient who has been in the Orient or certain tropical areas should suggest pulmonary paragonimiasis. The disease may be encountered in Americans who have been in endemic areas during military operations. Paragonimiasis is usually contracted by eating raw or poorly cooked fresh water crustaceans such as crabs and crayfish but may follow the drinking of contaminated water. The oriental lung fluke, *Paragonimus westermani*, within the lung parenchyma produces a disease called endemic hemoptysis, lung distoma, or pulmonary distomiasis. The symptoms and signs depend upon the stage of the disease; the typical features are (*1*) hemoptysis, (*2*) the presence of opercular eggs in the sputum, and (*3*) positive findings in the chest roentgenogram. The predominant hemoptysis is usually in intermittent, brief episodes, but the patients may produce rusty-brown sputum every day for weeks or months. Unless there is secondary infection, the sputum is thin, mucoid, or watery with short, stringy particles of tenacious, gelatinous material. These dark or reddish-brown particles account for the sputum's rusty-brown color and resemble small strands of tobacco or sand at the bottom of the sputum cup. The particles are aggregates of *Paragonimus* ova. Sputum production at times may be as voluminous as in bronchiectasis. If there is secondary infection, the sputum may be purulent. Shortness of breath, fever, malaise, fatigability, and anorexia may be present in patients with extensive pulmonary involvement, but there is no chronic cough. The patient usually coughs only in a conscious effort to expel material from the lungs. In the uncomplicated disease, the temperature is normal or rarely above 100° F., and other evidences of toxicity are observed chiefly in patients with coexistent illness; the patients

most often appear surprisingly healthy, well-nourished, and unaffected by the disease. There are no typical roentgenographic findings, but the disease mimics pulmonary tuberculosis so closely that *Paragonimus* infestation should probably be considered only when the chest films suggest tuberculosis. The most common finding is a linear, patchy infiltration, chiefly at the bases and periphery of the lung fields. In early cases, the density is not unlike that of exudative pneumonitis and tends to disappear with symptomatic improvement. A well-defined area of rarefaction, usually less than 8 mm. in diameter, frequently occurs within a linear density. It is better described as "cystoidal" rather than "cavitary" since it is produced by the burrowing of the organism with reactive fibrous tissue production. The disease is extremely benign, and the diagnosis may be made only incidentally while investigating some unrelated complaint. Secondary anemia does not usually develop, even after many years of periodic hemoptysis. Although pulmonary lesions constitute the primary pathologic process, virtually every organ system can be involved. There is no known therapeutic agent but various drugs have been tried; notably, tartar emetic, emetine, Lipiodol, and Prontosil. In a few cases, intramuscular Fuadin has given inconclusive but encouraging results. Pneumoperitoneum has controlled profuse pulmonary hemorrhage in one case. In patients seen in Korea, the initial response to the intermittent administration of emetine was encouraging. Symptomatic improvement, with reduction in sputum production, hemoptysis, and ova in the sputum, was observed almost without exception. In some cases, ova disappeared from the sputum and the chest roentgenogram improved. This regression was short-lived; symptoms recurred, ova again appeared in the sputum, and pulmonary infiltrations became more evident within one to three weeks after therapy was discontinued.—*Pulmonary paragonimiasis: A review with case reports from Korea and the Philippines, F. T. Roque, R. W. Ludwick, & J. C. Bell, Ann. Int. Med., June, 1953, 39: 1206.*—(*T. H. Noehren*)

**Endobronchial Blastomycosis.**—In 7 patients treated during the past five years for pulmonary *Blastomyces dermatitidis*, endobronchial lesions were seen on bronchoscopy during an active phase of the pulmonary disease, and in 2 patients the findings were confirmed pathologically. The most common bronchial lesions were superficial ulcerations with a characteristic type of retained secretion in the involved bronchial segments. Bronchoscopy may aid diagnostically, both by revealing such changes and by providing material for laboratory investigation. Pulmonary resection may prove gratifying in eradicating localized pulmonary lesions due to *B. dermatitidis*, and healing of the bronchial stump was satisfactory in 2 such cases. The infection was always systemic and not a localized pulmonary process. Roentgenographically, the lesions included diffuse exudative disease, lobar atelectasis, cavity formation, and pleural involvement with effusion. In the quiescent or healing phase, fibrotic, strandlike residues were the most common findings. The cases reported here responded favorably, at least temporarily, to iodide therapy including administration by the aerosol route.—*Endobronchial lesions in pulmonary blastomycosis, W. Weisel & F. B. Landis, J. Thoracic Surg., June, 1953, 25: 570.*—(*R. E. MacQuigg*)

**Berylliosis.**—From 1940 to 1953, 431 patients with various manifestations of acute beryllium intoxication were observed and treated. There were 10 fatalities in the pneumonitis group. The details of exposure, urinalyses, and lung biopsies, analyses for beryllium, and other pertinent data were available for this group, as were tissue analyses for the element in 5 autopsied cases. Clinical and laboratory data were obtained on more than 75 patients who recovered from tracheobronchitis and pneumonitis. Beryllium assays were made on tissues from 2 patients who recovered from major acute respiratory mani-

festations, but who died later from other causes years after exposure. In the survey, no persons who recovered from acute pneumonitis developed a chronic or delayed form of berylliosis. Of the 8 instances of chronic berylliosis of occupational origin, one patient had a medically established diagnosis of acute tracheobronchitis, while 4 others gave histories suggestive of acute tracheobronchitis during brief occupational exposures to beryllium. In recent years, the incidence of cutaneous berylliosis among workers in the beryllium industry has been reduced from 25 to 2 per cent and the respiratory syndromes almost to zero by engineering and medical hygienic preventive measures. The eczematous type of dermatitis is caused by allergic sensitivity to beryllium compounds. Studies of beryllium patch tests on patients with both acute and chronic berylliosis, on controls, and in similar pathologic conditions suggest that (*1*) the entity is a hypersensitization, and (*2*) the patch test is an extremely important tool in differential diagnosis. Beryllium remains in body tissues and is excreted for many years after the patient has been removed from exposure. The survey gives some evidence that the excretion of beryllium decreases proportionally to the increasing interval since exposure. The presence of beryllium in body tissue and urine is indicative of past or recent exposure to beryllium. The amount detected by present analytic methods does not bear any relationship to the diagnosis of berylliosis per se or to the severity of the disease, if present. The integrated medical, safety, and industrial hygiene program has been largely responsible for the phenomenal decrease in the incidence of beryllium poisoning and the total elimination of deaths in the local extraction plants. Therapy is mainly symptomatic and conservative, although the recent experience with corticotropin and cortisone is encouraging in both the chronic and the acute manifestations.—*Berylliosis, J. M. DeNardi, H. S. Van Ordstrand, G. H. Curtis, & J. Zielinski, A. M. A. Arch. Indust. Hyg. & Occup. Med., July, 1953, 8: 1.*—(*T. H. Noehren*)

**Pulmonary Manifestations of Scleroderma.**—Scleroderma is a systemic collagen disease in which various organs may be involved. Pulmonary fibrosis may occur. Of 37 patients with the clinical diagnosis of scleroderma, 5 had abnormal chest roentgenograms. The roentgenologic findings consisted of diffuse, linear, interstitial infiltrations, more marked in the lower half of both lung fields. Pulmonary changes sometimes appeared earlier than the skin lesions of scleroderma. The chief pulmonary symptoms were dyspnea and cough. There was no correlation between the extent of the skin changes and the pulmonary involvement. The principal pathologic change in the lungs is a sclerosing alteration of the collagen framework, which interferes with the oxygen diffusion across the alveolocapillary membrane.—*Pulmonary manifestations of scleroderma, W. H. Shuford, W. B. Seaman, & A. Goldman, A. M. A. Arch. Int. Med., July, 1953, 92: 85.*—(*G. C. Leiner*)

**Diffuse Interstitial Fibrosis.**—Diffuse interstitial fibrosis of the lungs, described by Hamman and Rich, is rare and the diagnosis is established only after death by careful microscopic studies. One such case was correctly diagnosed before death by means of cardiac catheterization and lung biopsy studies. It was unusual that, early in the course of the illness, the patient had hypermetabolism which was erroneously interpreted and treated as hyperthyroidism. Later he developed heart failure, the symptoms of which dominated the clinical picture and overshadowed the underlying pulmonary disorder. Finally, cortisone therapy was instituted. The effects of this drug were studied microscopically by repeated lung biopsies. No real benefit was observed either clinically or microscopically.—*Diffuse interstitial fibrosis camouflaged by hypermetabolism and cardiac failure: Ante-mortem diagnosis with biopsy and catheterization studies, J. J.*

*Silverman & T. J. Talbot, Ann. Int. Med., June, 1953, 38: 1326.—(T. H. Noehren)*

**Localized Interlobar Effusion.**—Five cases of "vanishing tumor" of the lung were found within a year among 33,084 photofluorograms taken at a large general hospital. The individuals surveyed were chiefly hospital admissions, receiving ward and dispensary patients, and smaller groups of employees or hospital visitors. A "vanishing tumor" was suspected if there were an enlarged heart or abnormal cardiac silhouette and a density in the region of one or more of the interlobar fissures, especially on the right side. The diagnosis of localized interlobar effusion due to congestive heart failure was confirmed by the disappearance of the lesion as congestive heart failure improved with therapy. The lateral chest film helped determine whether a collection of fluid was in the plane of a fissure. Fluid in the oblique fissure tended to be hazier and less well-demarcated than an effusion in the transverse fissure on the posterior-anterior roentgenogram, since the former did not lie in a plane parallel to the direction of the roentgen rays. The response to therapy varied considerably, depending primarily on the vigor with which therapy was pursued. Other evidence of congestive failure generally disappeared earlier than the interlobar effusion did. The effusions were so deep in the fissures that they produced no physical signs; in some cases, frequent photofluorograms showed that a "vanishing tumor" was a subclinical manifestation of cardiac failure. Of the 5 patients, 2 died and were autopsied. The post-mortem findings supported the thesis that "vanishing tumor" of the lung occurs in patients with congestive heart failure and obliterative pleuritis.—*Localized interlobar effusion in congestive heart failure, W. Weiss, K. R. Boulot, & W. I. Gefter, Ann. Int. Med., June, 1953, 38: 1177.—(T. H. Noehren)*

**Mechanical Respirators.**—Either the intermittent positive or the positive-negative type of respirator may be safely employed in patients who are in an essentially normal circulatory state. In patients with respiratory and/or circulatory failure, intermittent positive pressure respirators may depress the blood pressure and cardiac output sufficiently to threaten the life of the patient. The use of the alternating positive-negative pressure respirator permits the administration of artificial respiration without endangering the circulation. Since the circulatory status of patients in need of artificial respiration is not uniformly good, it is recommended that a negative pressure phase be employed in mechanical respirators. Mechanical respirators employing alternating positive and negative pressures and having a mean mask pressure at least as low as atmospheric pressure are safe and effective means of producing artificial respiration.—*Importance of negative pressure phase in mechanical respirators, J. Maloney Jr., J. O. Elam, S. W. Handford, G. A. Balla, D. W. Eastwood, E. S. Brown, & R. H. Ten Pas, J.A.M.A., May 16, 1953, 152: 212.—(H. Abeles)*

**Mechanical Exsufflation.**—An attempt was made to simulate as much as possible the obstructive component present in clinical conditions which constrict the larynx, trachea, or bronchi. This was done by placing a 3 mm. orifice into the mouthpiece of a modified tank respirator. Studies were made on 8 young healthy volunteers. After normal values were determined, values were measured under obstructed conditions. These showed a diminution of inspiratory and expiratory volume flow rates, an elevation of alveolar $pCO_2$ and lowering of $pO_2$, a lowering of venous pressure, and a marked decrease in inspiratory intra-oral pressure. There was marked subjective dyspnea. With the obstruction still in place, values were again determined after three minutes of exsufflation. This consists of inflation of lungs with 40 mm. mercury of pressure followed by rapid (0.06 second) termination of pressure at the onset of the expiratory cycle. When this mechanism is applied, all values revert to normal or better than normal with relief of dyspnea. It is suggested that the use of ex-

sufflation would be of value in patients with obstructive lesions in the respiratory tract.—*Physiological effects of mechanical exsufflation on experimental obstructive breathing in human subjects, R. M. Cherniock, C. A. Gordon, & F. Drimmer, J. Clin. Investigation, December, 1952, 31: 1028.*—(*S. J. Hadley*)

**Oxygen-Aerosol and Postural Drainage.**—Mortality studies of newborn infants indicate a high incidence of respiratory obstruction complicated by pneumonia. The use of an oxygen-rich, supersaturated atmosphere combined with postural drainage restores physiologic drainage of the bronchopulmonary tree. "Mist-$O_2$-Gen," a new apparatus for continuous aerosol treatment, can be used with postural drainage during incubator care. Wetting agents in aerosol solutions apparently aid in combating atelectasis and deserve further investigation.—*Mist-$O_2$-Gen therapy and postural drainage for respiratory difficulties of the newborn infant, R. Denton & C. D. Ross, J. Pediat., May, 1953, 42: 551.*—(*M. J. Small*)

**New Continuous Nebulizer.**—A detergent aerosol solution (Alevaire) is effective, nontoxic, and reliable for dissolving viscid bronchopulmonary secretions. A new continuous nebulizer (Alevizer) produces a satisfactory mist and is small enough to place within an incubator or tent; alternatively, the aerosol can be piped in from the Alevizer to the enclosure. The Alevizer can be employed with either oxygen or compressed air and there is a portable compressed-air humidifying unit for home or hospital use (Author's summary).—*A new continuous nebulizer (Alevizer) for humidification and Alevaire therapy, J. B. Miller, J. Pediat., June, 1953, 42: 721.*—(*M. J. Small*)

**Tietze's Syndrome.**—Among 3 cases of Tietze's syndrome, 2 occurred in patients with Hodgkin's disease, the third one in an apparently healthy person. Tietze's syndrome is a benign, self-limiting disease characterized by tender, nonsuppurative swelling of the upper costal cartilages. Usually, one of the second costal cartilages is involved; multiple involvement of costal cartilages is uncommon. Pain usually persists for a few days to a few weeks, while swelling may continue for months or even years. Nontuberculous respiratory disease or rheumatic conditions frequently precede or accompany the syndrome. Its cause is not well known. On an anatomic basis, it is suggested that small tears or rheumatoid involvement of the inconstant interarticular sternocostal ligament may be an important factor in the etiology of Tietze's syndrome. It should be considered in the differential diagnosis of chest pain and of tumor of the chest wall.—*Tietze's syndrome, cause of chest pain and chest wall swelling, A. G. Motulsky & R. J. Rohn, J.A.M.A., June 6, 1953, 152: 504.*—(*H. Abeles*)

**Stress Fractures of Ribs.**—Two fractures of the ribs occurred in the last weeks of the first pregnancy and one fracture occurred toward the end of the second pregnancy in a woman who was otherwise healthy. All of the fractures were of the lower ribs and left-sided. (Author's summary).—*Stress fractures of ribs in successive pregnancies, K. Marsh, J.A.M.A., May 2, 1953, 152: 26.*—(*H. Abeles*)

**Traumatizing Effect of Scapula.**—In 3 cases of Maurer's combined thoracoplasty, the subsequent appearance of a characteristic cavity near the lower angle of the scapula suggested that the underlying lung tissue was traumatized by the movements of the intrathoracic scapula (Author's summary).—*Die traumatisierende Wirkung der intrathorakalen Scapula bei der Thorakoplastik, G. Mark, Schweiz. Ztschr. Tuberk., 1953, 10: 144.*—(*E. Dunner*)

**Exploratory Thoracotomy.**—In spite of the fact that all nonsurgical adjuncts were employed, establishment of a definite diagnosis required resort to exploratory thoracotomy in approximately 50 per cent of 356 cases of localized pulmonary lesions. Approximately 30 per cent of 180 lesions of pre-

viously undetermined nature proved, on exploration, to be bronchogenic carcinomas, while approximately 36 per cent were classified as granulomatous processes. The remaining lesions were distributed among a wide variety of diagnoses. There were 203 cases of bronchogenic carcinoma in all, and, among 37 patients without symptoms, there was only one inoperable carcinoma; whereas among the 166 patients with symptoms, there were 59 inoperable carcinomas. The hospital mortality in 356 cases in which thoracotomy was performed was 2.9 per cent for 138 cases of pneumonectomy, 5.4 per cent for 112 cases of lobectomy and segmental resection, 1.7 per cent for 59 cases of exploratory thoracotomy, and none in 47 cases of local excision. —*Exploratory thoracotomy in diagnosis and management of certain pulmonary lesions, P. E. Bernatz & O. T. Clagett, J.A.M.A., May 30, 1953, 152: 379.*—(*H. Abeles*)

**Errors in Diagnosing Cancer.**—Investigation of recent series of cases of carcinoma of the stomach and the lung from Charity Hospital of Louisiana, New Orleans, revealed a number of disturbing factors, including (*1*) no recent improvement in the duration of symptoms before medical consultations; (*2*) mistaken therapy, directed toward symptoms before causes were investigated, both within and without the hospital; (*3*) long delays in the hospital before the diagnosis was established and treatment instituted; (*4*) lack of diagnostic suspicion; and (*5*) the tendency, in a small number of cases, to resort to neuropsychiatric causes to explain symptoms of organic origin, often before any serious attempt at diagnosis had been made. The enumeration of these erroneous tendencies indicates methods of correcting them. Most important of all are: (*1*) maintenance of a high and constant index of suspicion; (*2*) the use of laboratory studies only as adjuncts to clinical observation; (*3*) the prompt use of exploratory thoracotomy and laparotomy as diagnostic measures; (*4*) the establishment of an incontrovertible diagnosis before either gastric or respiratory symptoms are treated by any method at all; and (*5*) constant stress upon the urgency of malignant disease, particularly to medical students (Author's summary).—*Certain preventable errors in the diagnosis and management of carcinoma of the stomach and the lung, F. F. Boyce, Ann. Surg., June, 1953, 137: 864.*—(*M. J. Small*)

**Pleural Mesothelioma.**—A 57-year-old man complained of pain in the right chest characteristic of an intercostal neuralgia. Physical examination was essentially normal except for clubbing of the fingers and osteo-articular changes of the upper extremities. These were discounted at the time because of an old history of rheumatism. Chest radiography demonstrated a large circumscribed mass in the right anterior thorax, connected by a pedicle to the costosternal junction. At operation, the mass was found to be the size of a tangerine. It was easily separated from the visceral pleura but intimately attached to the parietal pleura which overlay it, and was removed *en bloc*. On section, the tumor was found to consist of hard regions and cavitary areas. On microscopic examination, it was seen to be a fibrous mesothelioma. The patient recovered uneventfully and is alive and well four years later. The osteo-arthopathy gradually disappeared.—*Mésothéliome de la plèvre, M. A. Campo, Poumon, April, 1953, 9: 263.*—(*F. S. Lansdown*)

**Malignant Pleural Tumor.**—A 59-year-old man complained of exertional dyspnea with progressive weakness and was found to have a left pleural effusion. Thoracentesis yielded serofibrinous fluid containing 46 per cent lymphocytes. In the next three months, fluid re-accumulated rapidly, requiring repeated thoracenteses; the total volume removed was estimated to be 20 liters. A radiogram following a thorough thoracentesis showed a large, rounded mass which on lateral tomography was seen to lie against the left posterior chest wall. During the period between the initial thoracentesis and operation three months later, the patient remained asymptomatic and in excellent general

health. At operation the pleura was very thick; the mass was extrapleural and easily removed, as were 2 other smaller masses. Decortication was impossible, although there was no evidence of tumor in the thickened pleura. On microscopic study, the tumor was unquestionably malignant but showed different aspects in different sites, some appearing mesenchymatous and some epithelial. In some areas it looked myxosarcomatous and in others like a glandular cancer. Microscopically, the possibility that it was a metastatic tumor could not be ruled out, but its gross appearance and the site of origin indicated its pleural origin.—*Tumeur circonscrite de la plèvre pariétale, Lagèze, Latarjet, Chassagnon, Mayer, & Riffat, Poumon, April, 1953, 9: 257.*—(*F. S. Lansdown*)

**Pleural Mesothelioma.**—A 33-year-old woman had pain in the right arm and shoulder. Six years earlier a radiogram of the chest was said to have shown a "cyst of the right lung." A roentgenogram taken three years later revealed a circumscribed density in the right upper mediastinum. At the time of operation the mass occupied the upper half of the right hemithorax. The patient had Horner's syndrome and evidence of venous collateral circulation. At operation a huge hard mass filled the upper portion of the right hemithorax. The visceral pleura was free and the lung could be pushed away from it. The tumor was shelled out from the capsule except medially where it had invaded the mediastinum. On microscopic examination, it was cataloged as a primitive pleural mesothelioma. The patient is alive six months later, having had a course of radiotherapy, but is again having pain in the arm.—*Mésothéliome de la plèvre, J. B. G. Bengochea, Poumon, April, 1953, 9: 253.*—(*F. S. Lansdown*)

**Pulmonary Cysts.**—Pulmonary cysts are initially found as radiolucent areas without lung markings. Many are giant, emphysematous bullae which appear relatively suddenly. Others may be classified as: (*1*) true congenital cysts; (*2*) chronic interstitial pneumonitis with emphysema or chronic bullous emphysema; (*3*) cystic bronchiectasis; and (*4*) pulmonary pneumatoceles, localized alveolar or lobular ectasia, occurring with infection and a check-valve mechanism. Of 26 cases of pulmonary cysts, 20 were in men and 6 in women; their ages ranged from 18 to 69 years. On the basis of the nature of the bronchial communication and the functional state of the remaining lung, these cases may be divided into three groups. *Group I* included 5 patients with apparently normal lungs except for large air cysts which communicate with the bronchial tree. These patients overventilate what amounts to dead space and become dyspneic after relatively mild exertion. Physiologic studies revealed that: (*1*) the total lung volume is normal; (*2*) the maximum breathing capacity is relatively normal or slightly reduced; (*3*) the spirogram reveals only hyperventilation; and (*4*) the rate of oxygen removal is reduced at rest and during exercise, but the total oxygen consumption is within normal limits. The 6 patients in *Group II* had apparently normal lungs except for large air cysts with poor or intermittent bronchial communication. Physiologic observations revealed that: (*1*) the total lung volume is greatly restricted; (*2*) maximum breathing capacity occasionally is greatly reduced; (*3*) the spirogram shows evidence of expiratory obstruction and air trapping, with irregular respiratory movements; (*4*) moderate hyperventilation is present during exercise; (*5*) the index of pulmonary mixing is high or normal; (*6*) the total oxygen consumption and rate of oxygen removal are relatively normal; (*7*) arterial blood oxygen saturation and carbon dioxide tension are normal; and (*8*) bronchospirometry shows decreased vital capacity and oxygen intake in the affected lung whose ventilation is depressed to a lesser extent. The severe ventilatory insufficiency in these patients is due to the mechanical interference with the chest bellows. Normal residual air indicates the absence of emphysema in the remaining lung. *Group III A*, consisting of 5 cases, was characterized by air cysts with

poor or intermittent bronchial communication associated with chronic diffuse emphysema in the remaining lung. Physiologically, (*1*) the total lung volume is reduced and the residual air is increased; (*2*) the maximum breathing capacity is severely restricted but improves with bronchial dilator drugs; (*3*) the spirogram shows expiratory slowing and air trapping; (*4*) hyperventilation occurs during standard exercise as well as in the recovery period; (*5*) the index of pulmonary mixing is usually high; (*6*) the total oxygen consumption, rate of oxygen removal, and arterial respiratory gas contents are relatively normal; and (*7*) bronchospirometric examination shows that the affected lung contributes its predicted share to the total vital capacity, total ventilation, and total oxygen consumption. The two main difficulties are related to the interference with ventilation imposed by the relatively noncollapsible air sac and the large amount of residual air associated with the emphysema. The 10 cases of *Group III B* are characterized by air cysts with poor or intermittent bronchial communication associated with chronic diffuse emphysema in the remaining lung. The disability is due to both ventilatory and alveolar respiratory insufficiency. There was (*1*) a greatly reduced total lung volume with increased residual air; (*2*) greatly reduced maximum breathing capacity, less than 20 per cent of the predicted value in 3 of 5 cases; (*3*) spirographic evidence of air trapping and expiratory obstruction; (*4*) hyperventilation in patients with the highest breathing capacities and hypoventilation in those with greatly limited breathing capacities; (*5*) abnormally high index of intrapulmonary mixing in 3 cases; (*6*) reduced oxygen consumption during exercise in those patients unable to hyperventilate; (*7*) arterial anoxia following exercise. Patients in this group are more incapacitated than those in *Group III A* because they have low oxygen and high carbon dioxide tensions in the alveolar air which is reflected to various degrees in the arterial blood. Therapy is directed toward preventing and treating complications, and the lesions are removed if possible. Respiratory infection is controlled with antibiotics and chemotherapy. Bronchodilator drugs are used to improve drainage and breathing capacity. Oxygen therapy must be used with discretion. It may benefit the patient by: (*1*) decreasing the cardiac output by relieving the anoxemia stimulating the heart; (*2*) possibly reducing right ventricular strain by vasodilatation in the pulmonary bed; (*3*) decreasing the cellular damage due to anoxia. The hazards of oxygen therapy must be kept in mind: (*1*) Withdrawal of the anoxemic stimuli to the cortex and medulla may depress the cortical cells. (*2*) Respiration may be depressed with further accumulation of carbon dioxide. (*3*) Reduced hemoglobin takes up more carbon dioxide than oxyhemoglobin. During oxygen therapy, there is increased oxyhemoglobin and, therefore, inpaired transport of carbon dioxide. (*4*) Neurologic changes during oxygen inhalation by anoxemic patients have been attributed to an abrupt rise in cerebrospinal fluid pressure, which reached 500 mm. of saline in some cases. Each of these chronically anoxic patients should be considered individually for oxygen therapy, limiting its use to specific indications. Certain principles should be followed in its administration: (*1*) Oxygen concentration should be limited to 40 to 60 per cent; (*2*) this should be intermittent rather than continuous; (*3*) consideration should be given to the use of gradually increasing oxygen concentration when high concentrations are necessary. Surgical removal of the pulmonary cysts is the most effective therapy but its usefulness varies with the different groups. In *Group I* patients, a lesion severe enough to interfere with the person's ability to follow his usual occupation should be removed as an elective procedure. In *Group II* patients, when conditions permit it, surgery is the treatment of choice. In *Groups III A* and *B*, diffuse pulmonary emphysema is present in addition to the large air sacs, and surgery is usually hazardous, if not impossible, and the patient often remains a respiratory cripple.—*Pulmonary air cysts: Some diagnostic, physiologic, and*

*therapeutic considerations, K. A. Harden, J. Nat. M. A., May, 1953, 45: 167.—(L. Hyde)*

**Pulmonary Agenesis.**—The death of some infants with congenital absence of one lung has been attributed to the anomaly alone since no other abnormalities were noted at autopsy. A possible cause of such deaths was suggested by the findings in a case of pulmonary agenesis in which a thoracotomy was performed because of progressive respiratory difficulty. The operative findings together with the later post-mortem observations indicated that there was partial intermittent obstruction of the airway. The autopsy findings alone probably would not have provided the correct interpretation of the clinical course because the vascular compression of the tracheobronchial tree was evident only at operation. The infant showed only slight respiratory symptoms during the first few weeks of life. The episodic cyanosis and respiratory distress of gradually increasing severity occurred. Usually when the infant slept, no respiratory difficulty was noted. Crying, however, resulted in a rapid and alarming change in the infant's condition with deep cyanosis. The anatomic findings suggest that, when crying increased the intrathoracic pressure, the airway was compressed by the aorta and an anomalously placed pulmonary artery interfered with ventilation. The condition was not amenable to surgical correction.—*Agenesis of the lung with vascular compression of the tracheobronchial tree, H. C. Maier & W. J. Gould, J. Pediat., July, 1953, 43: 58.—(M. J. Small)*

**Supervoltage Roentgenotherapy of Esophageal Carcinoma.**—Between 1940 and 1952, 58 patients with carcinoma of the esophagus were seen. Of 27 adequately treated with supervoltage roentgenotherapy, and of 39 in whom treatment was started, 5 are clinically well today. Among 22 patients adequately treated but uncontrolled, almost or quite normal esophageal function persisted until shortly prior to death in 8 instances. Analysis of these 22 cases suggests that in only one of them surgery may possibly have offered a better chance.—*Results of supervoltage roentgenotherapy of esophageal carcinoma, F. Buschke & S. T. Cantril, J. Thoracic Surg., July, 1953, 26: 105.—(R. E. MacQuigg)*

**Anomaly of Pulmonary Veins.**—A white girl was born weighing 1,120 gm. She was cyanotic, especially after feedings, and died seventeen days after birth. Autopsy showed a patent foramen ovale, a defect measuring 5 by 7 mm. in the upper portion of the interventricular septum, and a patent ductus arteriosus. The pulmonary veins combined to form a common pulmonary vein, which passed through the diaphragm to empty into the ductus venosus within the liver and thence into the inferior vena cava. This is the fourth case described in which all of the pulmonary veins emptied into the ductus venosus.—*Drainage of pulmonary veins into ductus venosus with other anomalies, H. D. Specht & A. F. Brown, A. M. A. Arch. Int. Med., July, 1953, 92: 148.—(G. C. Leiner)*

**Septal Defects with Transposition of Pulmonary Veins.**—A safe and simple technique for correcting completely an atrial septal defect associated with transposition of the pulmonary veins of the entire right lung was used in 2 patients. The successful repair of the defects was proved by cardiac catheterization which revealed no postoperative evidence of a significant left-to-right shunt noted preoperatively. Since the introduction of cardiac catheterization and angiocardiography, this lesion is recognized more often during life. The anomalous pulmonary venous drainage into the right antrium or superior vena cava is demonstrated during cardiac catheterization by passing the catheter directly from the atrium or cava into the vessel or vessels. The diagnosis may be suspected when the superior or inferior caval blood has a higher oxygen content than the right atrial blood; or when there is a higher oxygen content in the right atrium than in the inferior or superior vena cava. Although anomalous drainage of one or more pulmonary veins may be of little consequence, such drainage of an entire lung is a

serious lesion. When both lungs drain into the right atrium or its tributaries, patients die very early unless there is also large atrial septal defect. In such cases, the septal defect permits some blood to enter the left side of the heart. Eventually, secondary changes take place in the pulmonary vessels, causing an increase in the pulmonary vascular resistance. This will tend to elevate the pulmonary arterial pressure and further increase the work of the right ventricle, ultimately leading to its failure. The need for correction of this congenital cardiac lesion is self-evident.—*The surgical correction of atrial septal defects associated with transposition of the pulmonary veins, W. B. Neptune, C. P. Bailey, & H. Goldberg, J. Thoracic Surg., June, 1953, 25: 623.*—(*R. E. MacQuigg*)

**Pulmonary Arteriovenous Fistula.**—Hereditary hemorrhagic telangiectasia was diagnosed in a patient who had been treated for epistaxis for twenty-three years. Hemoptysis developed when the patient was 41 years old, and roentgenograms revealed a nodular mass indicative of an arteriovenous fistula. Surgical treatment was refused, and one year later, without warning, fatal hemoptysis occurred. Since fistulas may develop in areas of the lung previously considered to be normal, it is essential that unnecessary resection of pulmonary tissue be avoided. Segmental resection would appear to be the treatment of choice for this disorder.—*Fatal hemoptysis from pulmonary arteriovenous fistula: Report of a case in a patient with hereditary hemorrhagic telangiectasia, H. Israel & E. Gosfield, Jr., J. A. M. A., May 2, 1953, 152: 40.*—(*H. Abeles*)

**Cardiopulmonary Function Tests.**—In determining cardiac output, Fick's method may give too great an error (15 per cent) and too much physiologic variation. The arterial-venous oxygen difference is a more reliable test of an adequate circulation, and pressure measurements are of the highest clinical importance. Classification of mitral stenosis by the pressure in the pulmonary artery at rest and during effort is more objective and probably of more value than the criteria of the New York Heart Association. Analysis of oxygen saturation and tension during hyperventilation and in pulmonary capillary blood reveals that only the oxygen tension of arterial blood has value as a test of pulmonary function. In 29 normal persons and 108 patients with pulmonary disease whose arterial $pO_2$ was investigated at rest and during effort, a small oxygenating insufficiency was not more pronounced during effort. Bronchospirometry shows an increased oxygen uptake of the lower lung if performed in the lateral position and may be used as a function test. If the diseased lung does not increase its oxygen uptake when lowermost, it has little reserve function. Bronchospirometry has shown that there is a tremendous loss of function in pleural disease and after an intrapleural pneumothorax has been abandoned. Extrapleural pneumothorax causes only slight impairment. After lobectomy approximately one-third of the total function remains on the operated side; a segmental resection may not cause a significant decrease of pulmonary function. Decortication may improve pulmonary function considerably. The best of all pulmonary function tests is the operation itself. The following pulmonary function tests ought to be done in the order listed: (*1*) In cases of pulmonary tuberculosis, evaluation of all roentgenograms from the very beginning of the disease gives the most important information about pulmonary function. (*2*) Clinical investigation is important but will not necessarily give the desired information. Pronounced dyspnea at rest is a bad sign. (*3*) Ventilation is investigated by determining maximal breathing capacity and ventilatory reserve; in most cases these investigations are sufficient. (*4*) In cases of ventilatory insufficiency, oxygen and carbon dioxide tension in the arterial blood ought to be performed, both at rest and during voluntary hyperventilation. (*5*) The residual capacity may give valuable information. (*6*) Bronchospirometry is most valuable in many cases but should not be performed in tuberculous pa-

tients with large cavities and considerable expectoration. In patients with tuberculosis the bronchospirometry should, if possible, be performed at the time of the operation when the double lumen catheter is introduced for endobronchial anesthesia and to prevent spillover. (7) According to Carlens, Hanson, and Nordenstrom, the most physiologic way to determine if the patient will withstand pneumonectomy is occlusion of the pulmonary artery. This is of value when the remaining lung has impaired function. The present pulmonary function tests may determine if a patient can withstand an operation but their further prognostic value is not yet known.—*Cardiopulmonary function tests, V. O. Björk, J. Thoracic Surg., July, 1953, 26: 67.*—(*R. E. MacQuigg*)

**Arterial Oxygen Test of Pulmonary Function.**—The efficiency of pulmonary function may be evaluated by estimating the content of the oxygen and carbon dioxide in the arterial blood, provided cardiovascular disorders can be excluded. The ventilation, the ventilatory reserve, and the arterial blood gases were investigated at rest and during effort in 29 normal individuals and 108 patients with pulmonary disease. The arterial oxygen tension ($pO_2$) method was much superior to the saturation method for determining small changes in the arterial blood. The $pO_2$ determination could be used to demonstrate that a cardiac catheter is in position for reading the "pulmonary capillary pressure." A significant correlation was found between the maximal breathing capacity and the arterial $pO_2$ at rest both in men and women, as well as between the ventilatory reserve (100-MV effort/MBC) and the arterial $pO_2$ at rest. There was a significantly lower arterial $pO_2$ in patients with a high residual capacity. When the resting arterial $pO_2$ was low, the $pO_2$ during effort was low as well. Effort had no significant influence on the arterial $pO_2$ in patients with a low pulmonary reserve. This may have been due to hyperventilation during effort so that a significant change in the arterial $pO_2$ during effort could not be used as an index of the pulmonary reserve. The resting arterial $pO_2$ was a good indication of the pulmonary reserve and therefore used as a test of lung function.—*The arterial oxygen tension in rest and during effort as a test of pulmonary function, V. O. Björk, P. A. Michas, & L. G. Uggla, J. Thoracic Surg., June, 1953, 25: 558.*—(*R. E. MacQuigg*)

**Ventilation in Mitral Stenosis.**—Pulmonary function studies were performed in 62 patients with rheumatic heart disease in whom mitral stenosis was the predominant valvular lesion. The patients were classified according to the New York Heart Association criteria for functional limitation. Patients with asymptomatic mitral stenosis had normal ventilatory functions except for occasional increases in resting minute ventilation and ventilatory equivalents. As symptoms appeared and progressed the following changes were noted: (*1*) There were gradual reductions in maximal breathing capacity and total vital capacity. (*2*) The timed capacities were not greatly reduced. (*3*) Resting minute ventilation, respiratory rate, and ventilatory equivalents rose slightly, while tidal volumes decreased. (*4*) The calculated mean effective alveolar ventilation was maintained throughout all stages of disability. The breathing reserve at rest and the walking index were not much affected until disability was severe. Patients not infrequently complained of weakness, fatigue, or dyspnea during exercise without showing diminished breathing reserve or increased dyspnea indices (Authors' summary).—*Ventilatory studies in mitral stenosis, N. R. Frank, D. W. Cugell, E. A. Gaensler, & L. B. Ellis, Am. J. Med., July, 1953, 15: 60.*—(*T. H. Noehren*)

**Thrombo-Embolism.**—Intravenous clotting has been divided into two main types, phlebothrombosis and thrombophlebitis. Phlebothrombosis may be further subdivided into (*1*) the malignant type, which produces most fatal pulmonary emboli; (*2*) the slowly progressive type, which is responsible for most nonfatal pulmonary emboli; and (*3*) the benign

type, which is seldom of medical or surgical significance. Thrombophlebitis may also be subdivided into (*1*) thrombophlebitis, (*2*) thrombophlebitis with phlebothrombosis, and (*3*) suppurative thrombophlebitis. Thrombophlebitis is easily recognized; it is manifested by progressive edema, pain in the leg, fever, and increased pulse rate. Phlebothrombosis is practically devoid of symptoms; usually the first indication is the postoperative development of pulmonary embolism. There are no premonitory signs in fatal pulmonary embolism in 45 to 82 per cent of the cases. The etiology of intravenous clotting is still unknown and probably includes local and general factors. The incidence of thrombosis seems to have increased; the unproved diagnoses account for the supposed increase in phlebothrombosis. The incidence of fatal pulmonary embolism rises and falls every ten to fifteen years. In approximately 3 per cent of all patients having laparotomies, thrombosis develops in the veins below the diaphragm. Pulmonary emboli develop in 8 to 16 per cent of these and approximately 7 per cent of surgical deaths are due to fatal emboli. Treatment is both prophylactic and curative. Definitive treatment consists of (*1*) vein ligation proximal to the thrombus, (*2*) administration of anticoagulants to stop thrombus formation, and (*3*) use of highly purified trypsin intravenously to dissolve the thrombus.—*Thrombo-embolic phenomenon—a local process with regional spread and systemic complications, M. Gage, Ann. Surg., May, 1953, 137: 577.*—(*M. J. Small*)

## ANTIMICROBIAL THERAPY

**Antimicrobial Therapy.**—Clinical investigative studies have been conducted on 875 patients with moderately advanced or far advanced pulmonary tuberculosis during the past six years at Fitzsimons Army Hospital using streptomycin, *p*-aminosalicylic acid (PAS), amithiozone, viomycin, oxytetracycline (Terramycin), and isoniazid, either alone or in various combinations. Intermittent streptomycin therapy equals the therapeutic effectiveness of daily streptomycin and is accompanied by less drug toxicity and a lower incidence of streptomycin-resistant organisms. The combination of intermittent streptomycin and daily PAS is one of the most effective drug regimens available today. The administration of PAS every third day does not protect against the emergence of streptomycin-resistant bacilli. Combined drug therapy is more effective than any given antimicrobial agent employed singly and, with the exception of amithiozone and streptomycin, is accompanied by a decreased incidence of drug resistance to either antimicrobial agent. Amithiozone has a relatively high toxicity and low therapeutic effectiveness; this drug deserves little place in the treatment of tuberculosis. Limited studies on viomycin and oxytetracycline reveal definite therapeutic effect, and the combination of either of these agents with streptomycin nearly equals results obtained with the combination of streptomycin and PAS. The high incidence of toxicity, although usually of minor nature, limits the clinical use of viomycin and oxytetracycline. Preliminary studies with isoniazid are most encouraging, but this drug should not be employed alone because of frequent drug resistance. When combined with streptomycin this disadvantage is minimized, but further experience is necessary with this regimen prior to unqualified recommendation. Drug therapy is most effective against disease of recent origin, less than six to twelve months' duration. Duration of drug treatment is not well defined at present but it is believed that antimicrobials should be administered for three to six months following maximal roentgenographic clearing and cavity closure with consistently negative cultures: thus, most patients with extensive caseous pneumonic disease will require eight to twelve months or longer of continuous drug therapy. Although the results of drug therapy are often dramatic, it is frequently not definite in a curative sense and must be integrated with an over-all program of bed rest, as well as medical collapse or surgical measures as the individual case dictates (Author's summary).—*Antimicrobial therapy, C. W. Tempel, F. W. Pitts,*

*& W. E. Dye, Ann. Int. Med., July, 1953, 39: 61.—(T. H. Noehren)*

**Isoniazid Therapy.**—Isoniazid was given to 126 patients with pulmonary tuberculosis between May and September, 1952, at a French military hospital. The usual daily dose was 4 to 5 mg. per kg. In 15 cases, isoniazid was administered intravenously in combination with *p*-aminosalicylic acid (PAS). The treatment period ranged between two and five months. Doses exceeding 6 mg. per kg. provoked marked nervousness. There were 3 cases of anuria, 2 of which were benign and transient; the third case was so severe that medication was discontinued. Constipation was present in 10 per cent of the patients at the onset of treatment. No other manifestations of toxicity were noted. The clinical results were remarkable, particularly in patients initially in poor general condition. There was usually a weight gain of several kilograms and an improved appetite at the beginning of therapy. All of the patients experienced a sense of well-being and euphoria. In most cases, cough and expectoration were markedly decreased. Among 85 patients treated with isoniazid alone there was complete roentgenographic clearing in 25 per cent, marked regression with disappearance of cavities in 18 per cent, diminution of cavities and moderate decrease of infiltrations in 30 per cent, poor or no results in 22 per cent. Poor results were obtained in 6 patients treated with isoniazid and streptomycin. Among the 15 patients given isoniazid and PAS intravenously, complete roentgenographic clearing occurred in 9 (60 per cent) and considerable improvement in 6 (40 per cent). In 20 patients, isoniazid was given with streptomycin and PAS; the results were excellent in 15 per cent, good in 45 per cent, and poor or absent in 40 per cent. One case of miliary tuberculosis treated with isoniazid alone showed complete roentgenographic clearing after one month. Prior to the use of isoniazid, 50 per cent of tuberculous meningitis cases were cured with streptomycin and intravenous PAS. All of 9 new patients with meningitis who were treated with streptomycin, PAS intravenously, and isoniazid recovered and the time required for cure seemed shorter than with the previous medication. Isoniazid administered intrapleurally in 3 cases of tuberculous empyema had a definite and rapid effect. Isoniazid had no roentgenographic effect on long-standing fibrocaseous pulmonary tuberculosis, but the concomitant use of the three agents produced marked clearing in a few of these cases. Among the 90 patients treated with isoniazid for recent, more or less extensive cavitary-nodular tuberculosis, 10 showed complete disappearance of the nodular and cavitary elements within a few months, 13 had clearing of nodular infiltrations and filling-in of the cavity; 18 showed diminution in cavity size and regression of infiltrations; and 49 had no results. No effect was seen with isoniazid in primary tuberculosis or in pleurisy with effusion.—*L'isoniazide dans le traitement des differentes formes de l'infection tuberculeuse, A. Duroux, P. Masson, J. Marty, H. Lacrampe, A. Jarnion, Galy, & Laurens, Rev. de la tuberc., 1953, 17: 95.—(V. Leites)*

**Early Results with Isoniazid.**—The early results of isoniazid therapy were evaluated in 414 patients after a minimum of three months of treatment. If the apparent onset of the disease occurred less than six months before treatment, the tuberculosis was considered "fresh," as in 146 cases; if the interval since the onset was longer, the tuberculosis was classified "old", as in 215 cases. Of the latter, 195 patients had received previous antimicrobial therapy and two-thirds had had collapse. A final group contained 53 cases of reactivation of arrested processes. Isoniazid was used alone, without collapse procedures, in daily oral doses of 5 mg. per kg. for 266 patients, 4 mg. per kg. for 116, and 6 to 7 mg. per kg. for 32 patients. Side effects were infrequent and insignificant, with nausea and constipation, in 31 cases; headache, insomnia, or paresthesias in 31 cases; albuminuria in 19 cases; transient fever and bronchial hypersecretion in 7 cases; and transient skin erup-

tions in 5 cases. Therapy had to be discontinued in only 6 cases; for hemoptyses in 2, hyperlipemia and hypercholesteremia in 2, and acrodynia in 2. Marked clinical improvement occurred in 75 per cent of patients with "fresh" lesions and in 39 per cent of those with "old" disease. Expectoration decreased or ceased in 76 per cent of the "fresh" cases and in 40 per cent of the "old" ones. Of the patients with fever, 25 per cent did not respond to isoniazid after three months; favorable results were obtained in the remaining 75 per cent. Complete defervescence occurred in only 68 per cent of patients with "fresh" and in 53 per cent of those with "old" disease. After three months, 54 per cent of the patients with "fresh" disease and 33 per cent with "old" disease had gained weight. Roentgenographically, lesions occupying less than one-sixth of the pulmonary parenchyma and with no cavity larger than 1 cm. in diameter were considered "slight"; those occupying less than one-third without cavities larger than 4 cm. were of "moderate" extent. A decrease in the extent of lesions by more than one-half was designated "marked improvement." Of the 194 "fresh" cases, 5 per cent progressed roentgenographically during therapy; 16 per cent remained unchanged; and 79 per cent improved, including 49 per cent markedly improved. Of the 210 cases of "old" tuberculosis, 10 per cent became worse; 39 per cent were unchanged; and 51 per cent were improved, including 16 per cent markedly improved. "Fresh" lesions were markedly improved in 56 per cent of the moderately extensive and in 40 per cent of the far advanced groups. In "old" tuberculosis, marked improvement occurred in 21 per cent of the moderately advanced and in 14 per cent of the far advanced groups. Of the "fresh" moderately large cavities, 57 per cent markedly improved as compared to 16 per cent of "old" large cavities. Among "fresh" cases, bacteriologic results were positive in 83 per cent before treatment and in 23 per cent after three months. Positive results decreased from 84 to 60 per cent in "old" cases. Sensitivity studies were done in only a few cases. Before treatment, 86 per cent of 42 patients had organisms sensitive to 0.1γ of isoniazid per ml. At the end of the third month, only 6 per cent of 32 patients had sensitive strains.—*Traitement de 414 tuberculeux pulmonaires par l'isoniazide, étude par les chefs de service de phtisiologie avec le concours de l'Institut National d'Hygiene: Rapport preliminaire, Mlle. A. Lotte & Mme. J. Poussier, Rev. de la tuberc., 1953, 17: 1.—(V. Leites)*

**Distribution of Radioactive Isoniazid.**—Four experiments in 3 patients were carried out with the use of isoniazid labeled with radioactive carbon ($C^{14}$) in order to obtain a better understanding of the distribution and excretion of isoniazid in the tuberculous patient. The first patient had pulmonary tuberculosis treated with wedge resection of residual caseous foci; the second patient had tuberculous cervical nodes which were resected; and the third one had a pleural effusion. The experiments show that isotopically labeled isoniazid is rapidly absorbed into the blood stream after intramuscular injection. Peak blood concentrations are found in the first hour, followed by a rapid fall in blood concentration during the first eight hours. Measurable amounts of isoniazid in blood and plasma can be demonstrated three to seven days after a single intramuscular injection. Isoniazid is freely diffusable and is found in all tissue and body fluids, including cerebrospinal fluid, after intramuscular injection. Appreciable concentrations were found in all tissue studied at the end of three and one-half and five hours, and there is indication that some tissue concentrations fall more slowly than blood concentrations. The highest concentrations found in normal tissues in man were in lung and skin. Isoniazid diffuses freely into dense, caseous lesions in both lung and lymph nodes and is present in high concentration three to five hours after injection. The drug is found in pleural fluid in high concentration two and one-half hours after injection, and measurable quantities remain three days later. Isoniazid is excreted chiefly by the

kidneys, with small amounts excreted in the feces and by the lungs as carbon dioxide. Following a single dose, most of the drug is excreted in twenty-four hours.—*Distribution and excretion of radioactive isoniazid in tuberculous patients, W. R. Barclay, R. H. Ebert, G. V. Le Roy, R. W. Manthei, & L. J. Roth, J. A. M. A., April 18, 1953, 151: 1384.—(H. Abeles)*

**Fate of Isoniazid.**—The dog was used to study the absorption, distribution, and excretion of isoniazid after both acute and chronic oral dosage in 34 animals. After single and repeated doses it was found that: (*1*) Peak plasma concentrations generally occur between thirty minutes and two hours after an oral dose of isoniazid. The thirty-minute plasma concentration is strictly proportional to the oral dose. (*2*) The average plasma disappearance rate of isoniazid is 19 per cent per hour. (*3*) Isoniazid is distributed uniformly in blood, cerebrospinal fluid, and most tissues. (*4*) There is no chemically detectable accumulation of the drug in body fluids or tissue even when the drug is given by mouth daily for two to eight months. (*5*) The urinary excretion reaches a peak between two and four hours and is complete in twenty-four hours. (*6*) From 44 to 86 per cent of the drug administered can be accounted for in the urine as isonicotinic acid plus unchanged isoniazid. These studies in the dog are similar to those reported in man.—*Absorption, distribution and excretion of isoniazid (Nydrazid) in the dog, B. Rubin & J. C. Burke, J. Pharm. & Exper. Therap., February, 1953, 107: 219.—(S. J. Hadley)*

**Bacillary Resistance to Isoniazid.**—Sputa from 161 tuberculous patients were studied for isoniazid sensitivity. Initially, the bacilli were fully susceptible in all. The bacilli from 25 patients became resistant to 5 γ of isoniazid per ml., those from 21 remained fully sensitive, and those from 9 became partially resistant (between 1 and 5 γ). There was very little difference between the two larger groups in duration of treatment or total dose. There was, however, a considerable difference in type of disease in that in the group becoming resistant larger, more numerous and older cavities were present. In certain patients whose bacilli had become resistant to streptomycin, the addition of isoniazid caused marked but temporary diminution of this resistance. A possible mechanism for this may be that in the mixed bacterial population the streptomycin-resistant organisms grow relatively poorly when deprived of streptomycin and under the influence of isoniazid. This would allow the few remaining streptomycin-sensitive organisms to grow in culture. As to indications for isoniazid therapy, they may be considered the same as for streptomycin in that resistance to the drug develops early in the same type of case. Streptomycin in association with isoniazid may be expected to delay resistance but not to prevent it.—*La résistance acquise par le bacille Koch au cours du traitement par l'isoniazide des tuberculeuse pulmonaires, A. Dufourt, J. Brun, J. Viallier, & H. Serre, Poumon, April, 1953, 9: 219.—(F. S. Lansdown)*

**Regression of Isoniazid Resistance.**—Pretreatment studies showed the tubercle bacilli of a patient to be sensitive to 0.2 γ of isoniazid per cc. Treatment with 5 mg. of isoniazid per kg. per day appeared effective until the forty-fifth day, when the sputum volume and its bacillary content increased. The microorganisms had become resistant to 20 γ of isoniazid. Treatment was discontinued on the sixtieth day. Three months later the tubercle bacilli were found to be sensitive to 1.0 γ of isoniazid. A similar result was obtained on repeated examination one month later. Similar regression of isoniazid resistance was noted in 3 other cases.—*La régression de la résistance a l'hydrazide isonicotinique (INH) des B. K. après l'arrêt du traitement, G. A. Nigoghossian, Schweiz. med. Wchnschr., February 28, 1953, 83: 218.—(E. Dunner)*

**Isoniazid Effects on Mycobacteria.**—The effect of isoniazid on *Mycobacterium tuberculosis* was studied electron-microscopically.

Under the trial conditions, morphologic changes were observed at the end of six hours and reached their climax twelve hours after the treatment was begun. After twenty-four hours there was complete disintegration of bacteria, and no further cultural inoculation was possible. During isoniazid treatment there was initially swelling of the bacteria, frequently followed by retraction and condensation of the protoplasm after the formation of an outer membrane. The condensed protoplasm was seldom expelled; there was usually intracellular plasmolysis with formation of "empty membranes" which finally disintegrated. There was seldom direct lysis of the bacteria. In regard to the "physiologic" mortality of tubercle bacilli, these findings differed in that during isoniazid treatment mortality of cells through the formation of empty membranes ("ghosts") occurred much more frequently than through direct lysis (Author's summary).—*Elektronenmikroskopische Untersuchungen über die Werkung von INH (Rimifon) auf die Tuberkelbazillen, H. Braunsteiner, F. Mlczoch, & W. Zischka, Schweiz. Ztschr. Tuberk., 1953, 10: 91.*—(*E. Dunner*)

**Streptomycin for Knee Tuberculosis.**—Five patients with synovial tuberculosis of the knee proved by demonstration of tubercle bacilli from aspirated joint fluid were treated with streptomycin. They have been followed for three to six years. All 5 patients did well. In none of the patients was osseocartilaginous tuberculosis observed before treatment, and in no case has there been any indication of osseocartilaginous erosion since institution of therapy. In one case in which arthrotomy was performed one year after streptomycin administration, there was no gross pathologic, bacteriologic, or histologic evidence of tuberculosis in the synovium, cartilage, or subchrondal bone.—*Effect of streptomycin in synovial tuberculosis of the knee, W. S. Smith & R. W. Bailey, J. A. M. A., June 27, 1953, 152: 792.*—(*H. Abeles*)

**Acetylcholine and Streptomycin.**—In cases of the so-called primary clinical resistance to streptomycin, an attempt was made to increase the therapeutic effect by altering the medium—in this instance, the patient. Thus, 29 patients with pulmonary tuberculosis were given streptomycin and acetylcholine alternately in order to create more favorable conditions and a certain lymphocytosis. Usually, acetylcholine and streptomycin or dihydrostreptomycin were administered on alternate days until 10 injections of acetylcholine were given. This twenty-day course was followed by the usual streptomycin therapy. Acetylcholine was useless in desperate and stationary cases and in exudative pleuritis. Of 23 remaining patients, 17 reacted more or less favorably. These observations and others in the literature indicate that increased parasympathetic tonus retards the development of pulmonary tuberculosis. Within limits, acetylcholine should be used in treating tuberculosis, especially in those rare cases in which tubercle bacilli do not respond optimally to the modern therapeutic means, so that even the slightest help may tip the scales in favor of the patient (Author's summary).—*Le système neurovegetatif et la tuberculose, R. Ferri, Schweiz. Ztschr. Tuberk., 1953, 10: 113.*—(*E. Dunner*)

**Local Streptomycin Reactions.**—The incidence of local pain from intramuscularly injected streptomycin salts was investigated in 65 patients. When the sulfate salt was used, none of the patients complained either spontaneously or on questioning. When the calcium chloride complex was administered, 3 patients complained spontaneously of pain at the site of injection, and 5 patients on questioning admitted having pain.—*Local pain from intramuscular injection of streptomycin calcium chloride complex, W. Long, W. Weiss, & S. C. Stone, J. A. M. A., May 2, 1953, 152: 25.*—(*H. Abeles*)

**PAS Hypersensitivity.**—A severe form of hypersensitivity to *p*-aminosalicylic acid

(PAS) which simulated mononucleosis or hepatitis was seen in 8 patients. In addition to fever, rash, lymphadenopathy, and lacrimation, a blood picture simulating early infectious mononucleosis and evidence of liver involvement was present in these patients. The symptoms subsided promptly on withdrawal of the drug and recurred upon readministration. A skin patch test with a 33 per cent ointment of PAS in lanolin was frequently positive.—*Severe para-aminosalicylic acid hypersensitivity simulating mononucleosis or hepatitis, M. R. Lichtenstein & W. Cannemeyer, J. A. M. A., June 13, 1953, 152: 606.*—(*H. Abeles*)

**Blastomycosis.**—A patient with systemic blastomycosis, including skin and pulmonary manifestations, was treated daily with intravenous administration of stilbamidine for twenty-nine days following a four-year period of observation and trial of standard forms of treatment. The dosage schedule consisted of 50 mg. of stilbamidine given in 100 cc. of 5 per cent glucose on the first day; 100 mg. of stilbamidine in 100 cc. of 5 per cent glucose on the second day; and on the third day to the twenty-ninth day, 150 mg. of stilbamidine was given daily in 500 cc. of 5 per cent glucose. Throughout treatment the patient received a low-purine, low-protein diet. There was no toxic reaction to stilbamidine. All cutaneous lesions and systemic symptoms disappeared following this therapy. The patient was able to resume his normal occupation during the entire post-treatment observation period of thirteen months.—*Treatment of blastomycosis with stilbamidine: Report of a case, H. Pariser, E. D. Levy, & A. J. Rawson, J. A. M. A., May 9, 1953, 152: 129.*—(*H. Abeles*)

**Fungus Infections and Antibiotics.**—In each of 5 cases of fatal fungus infections associated with antibiotic therapy, the diagnosis was confirmed by post-mortem examination. *Candida albicans* was the most common offending agent.—*Fatal fungus infection complicating antibiotic therapy, C. Brown Jr., S. Propp, C. M. Guest, R. T. Beebe, & L. Early, J. A. M. A., May 16, 1953, 152: 206.*—(*H. Abeles*)

**Penicillin Anaphylaxis.**—In 5 fatal and 4 severe reactions to penicillin, the major symptoms were urticaria, asthma, shock, cyanosis, and unconsciousness. Probably any type of penicillin, administered by any route, can produce this type of reaction. This type of sensitivity, unlike the delayed urticarial syndrome, is usually induced by repeated courses of penicillin and occurs more frequently in those persons who have other allergies. The immediate whealing skin reaction obtained with the scratch or intradermal test is diagnostic of the anaphylactic or atopic type of penicillin sensitivity. At the first sign of an immediate reaction, 0.5 to 1.0 cc. of epinephrine in a 1:1,000 dilution should be given intravenously. This should be repeated in two or three minutes if no improvement is seen. The intravenous administration of aminophylline may be indicated. Oxygen should be used to combat cyanosis and plasma for the treatment of shock if facilities are at hand.—*Penicillin anaphylaxis, nonfatal and fatal reactions, S. M. Feinberg, A. R. Feinberg, & C. F. Moran, J. A. M. A., May 9, 1953, 152: 114.*—(*H. Abeles*)

**Enhancement of Serum Chlortetracycline.**—Methods have been devised to increase the serum concentrations of chlortetracycline (Aureomycin) and oxytetracycline (Terramycin) up to tenfold after their oral administration to rats and guinea pigs. The most effective substances were citric and malic acids, although tartaric-acid, monosodium phosphate, and others were useful also. The effect was exerted over a wide range of doses, from 8 mg. to 200 mg. of chlortetracycline per kg. The citric acid was most effective when given with the dose of drug. The effect was apparent within an hour of administration and lasted at least eight hours. The mechanism of action is not understood.—*The enhancement of serum*

*levels of Aureomycin in experimental animals, H. J. Eisner, F. E. Stern, A. C. Dornbush, & J. J. Oleson, J. Pharm. & Exper. Therap., August, 1953, 108: 442.—(S. J. Hadley)*

## LABORATORY STUDIES

**Effect of Metabolites on Multiplication of Bacteria.**—Uncontrolled diabetes, starvation, and other conditions resulting in ketosis are commonly associated with abnormally great susceptibility to various infections, in particular to those caused by staphylococci and tubercle bacilli. Infection might be facilitated during ketosis by the additive effect of two independent factors: (*1*) the presence of ketone bodies in abnormally high concentrations, and (*2*) the decreased production of lactic acid at the site of inflammation. The present experiments on the effect of various metabolites on the survival and multiplication of microorganisms *in vitro* support this hypothesis. In order to approximate the conditions encountered by microbial agents *in vivo*, experiments were conducted in media consisting of balanced ionic solutions containing 0.5 per cent serum albumin and adjusted to acid reactions ranging from neutrality to pH 4.0. Various metabolites at different pH levels were then added and their effect on the multiplication of staphylococci and tubercle bacilli was noted. The organisms died very rapidly in acid media containing lactic acid in a concentration of 0.01 M or smaller; acetic, propionic, and butyric acids exerted a similar but less pronounced bactericidal effect. Under the same conditions, the microorganisms survived longer in the presence of polybasic acids, such as succinic, fumaric, and citric, and of glutamic acid. More particularly, they survived if ketone bodies such as dihydroxyacetone and pyruvic, beta-hydroxybutyric, alpha-ketoglutaric, and oxalacetic acids were added to the suspension fluid. Ketone bodies partly neutralized the antimicrobial effect of lactic and acetic acids, permitting growth even in a medium as acid as pH 5.3. Thus, lactic acid inhibits and ketone bodies stimulate the multiplication of staphylococci at the acid reactions which usually prevail in inflammatory areas, and this may explain in part the susceptibility to infection which is often associated with ketosis of various etiology.—*Effect of ketone bodies and other metabolites on the survival and multiplication of staphylococci and tubercle bacilli, R. J. Dubos, J. Exper. Med., August, 1953, 98: 145.—(J. S. Woolley)*

**Blood Medium for M. Tuberculosis.**—A medium for growing tubercle bacilli from small inocula consists of an agar base plus glycerine, out-dated human bank blood, and penicillin. Various concentrations of blood, glycerine, and penicillin were tested against the standard egg mediums of the American Trudeau Society, Corper-Cohn, Löwenstein, and Petragnani. Various dilutions of a suspension of *M. tuberculosis* H37Rv as well as serial dilutions of digested sputums from tuberculous patients were used as the inocula. Colonies were first noted approximately one week earlier, in all of the dilutions, on the blood than on the egg media. This may be due to the superior nutritional qualities of the blood, but it is also easier to detect the earliest growth against a blood-red background. The blood medium gave somewhat more sputum isolates than any of the others. The incorporated penicillin did not inhibit the growth of tubercle bacilli, even with the smallest inocula, nor was colonial morphology affected. The medium recommended contains 1.5 gm. of agar-agar, 1.0 ml. of glycerine, 30.0 ml. of human bank blood, 69.0 ml. of water, and 50 to 100 units of penicillin. The blood and penicillin are added to the autoclaved agar after cooling to 45° C. and just before tubing. When tightly sealed the tubes keep well in the refrigerator.—*Blood mediums for cultivation of Mycobacterium tuberculosis: V. Results with agar-agar basal medium and varying concentrations of blood, glycerine and penicillin, M. S. Tarshis, Am. J. Clin. Path., July, 1953, 23: 661.—(J. S. Woolley)*

**Plasma and Blood Agar for Tubercle Bacilli.**—Blood agar made from out-dated human bank blood has been recently recom-

mended as a substitute for egg medium for growing tubercle bacilli. In the present study plasma agar as well as the whole blood agar were prepared from blood and plasma obtained from out-dated bank blood. A small amount of malachite green was incorporated in the medium, which consisted of beef-heart infusion agar plus either 15 or 25 per cent whole blood or 15 per cent blood plasma. A concentration of malachite green (0.025 per cent) that had no effect on the growth of the bacilli in the whole blood media and in the egg medium used as a control completely inhibited growth in plasma agar. Even 0.0025 per cent malachite green in plasma agar slows the growth of bacilli. This inhibitory effect of the dye has also been reported when used with Dubos agar, which contains no egg. Comparative tests show that tubercle bacilli grow as well on the blood or plasma agar as on standard egg tubes (modified Löwenstein-Jensen). The medium described is recommended for small laboratories because it is considered easier to prepare than egg medium. —*Human plasma and blood agar for cultivation of tubercle bacilli, M. E. Clark, Am. J. Clin. Path., July, 1953, 23: 671.*—(*J. S. Woolley*)

**Pulmonary Blood Temperature.**—Studies in dogs showed that the rectal temperature was usually higher than the blood temperature of the pulmonary artery and the left atrium under environments of 20°C. and −18°C. The pulmonary artery blood temperature was higher than that of the left atrium in environments of 20°C. and −18°C. This difference was in the order of 0.01°C. in an environment of 20°C. and 0.03°C. in an environment of −18°C., with animals in the reclining state. When animals in an environment of 20°C. were suddenly exposed to an environment of −18°C., there was an increase for a short period of time in the pulmonary artery blood temperature, the left atrial blood temperature, and the rectal temperature. The cooling effect of the inspiration of cold air upon the blood in the pulmonary circulation is small (Authors' summary).—*Temperature changes of pulmonary blood during exposure to cold, G. W. Mather, G. G. Nahas, & A. Hemingway, Am. J. Physiol., June, 1953, 173: 390.*—(*G. C. Leiner*)

**Respiration and Venous Return.**—Venous return was recorded with a Pitôt-type differential flowmeter passed as a catheter via jugular vein into the superior vena cava of anesthetized dogs whose chests remained unopened. Direct measurement of volume flow in the superior cava demonstrated that application of intermittent positive-negative pressure respiration increased venous return significantly over that existing during intermittent positive-negative pressure respiration (Author's summary).—*Venous return during intermittent positive-negative pressure respiration studied with a new catheter flowmeter, G. A. Brecher, Am. J. Physiol., August, 1953, 174: 299.*—(*G. C. Leiner*)

**Respiration and Circulation in Blast Injury.**—By protecting the bodies of the experimental animals with the exception of their heads and by previous bilateral vagotomy and anesthesia of the carotid sinus, it has been possible to determine the origin of the respiratory and circulatory changes in rabbits exposed to the shock waves from a detonating high explosive. These experiments lead to the following conclusions: The changes in respiration and circulation are entirely or almost entirely of peripheral origin. Usually there seems to be no cerebral concussion component in the blast syndrome. The instantaneous acceleration of respiration is solely due to vagal reflexes elicited in the damaged lungs. Changes in circulation is of a twofold genesis. The initiation of the bradycardia and the blood pressure fall seem to be caused by the blast pressure acting externally on the carotid sinus region. The more prolonged effects, on the other hand, are due to reflexes evoked in the damaged lungs. This is especially marked as far as blood pressure is concerned (Authors' summary).—*Genesis of respiratory and circulatory changes in blast injury, C. J. Clemedson*

*& H. Pettersson, Am. J. Physiol., August, 1953, 174: 316.—(G. C. Leiner)*

## PUBLIC HEALTH AND EPIDEMIOLOGY

**Employment of Quiescent Tuberculosis Cases.**—It is hard for a physician to decide whether it is safe to advise employment of a person who has arrested or quiescent pulmonary tuberculosis, especially if the physician has had no training or experience as a tuberculosis specialist. It is also difficult for health authorities to formulate reasonable and correct principles covering such decisions. This matter was discussed at the First Congress of the International Union of Railroad Medical Services in November, 1950, and studied by the U. S. Department of Labor and the Veterans Administration. The decision is comparatively simple with two groups of applicants. In the first group, which can be employed at once without question, are persons whose roentgenograms show no evidence of recent or active tuberculosis. The physician can support his decision by such additional data as blood sedimentation tests, search for tubercle bacilli in gastric specimens, and tomography. In the second group, which should not be employed, are all applicants with progressive active lesions. These should not be in industry, both for their own safety and for that of other workers. In a third group are applicants whose condition requires careful pre-employment study. The authors would apply rigid tests in such cases: (*1*) Radiograms, including tomography, should show only quiescent lesions without cavitation or diffuse shadows suggesting exudation. (*2*) At least three negative cultures or animal inoculations should be obtained from gastric specimens taken at ten-day intervals. (*3*) Clinically, the temperature should be stable even after work; there should be no cough and expectoration except as they may persist in persons cured of tuberculosis who have become emphysematous or bronchiectatic; there should be normal pulse rates, respiratory rates at rest or after effort, and weight. (*4*) Biological tests, such as nonspecific sedimentation rate, should be considered. Candidates passing all of the tests may be recommended for provisional full employment provided they agree to have roentgenograms and gastric cultures every three months for three years. If the results of these examinations are satisfactory, they may be considered cured or arrested cases and treated as regular employees even in industries providing pensions and other special benefits. Applicants who have had effective pneumothorax should not be considered for permanent employment until three years after the pneumothorax has been discontinued; in the meantime, they may be employed temporarily. Unfortunately, another group of patients who are able to work present difficulties which have seemed insurmountable. These persons occasionally expectorate a few tubercle bacilli. The number of persons now employed is increasing, partly on account of better methods of detecting these "carriers." Refusal to employ them deprives industry of their services and them of their livelihood. They present little risk of infection because they do not cough. If refused employment by an industry having good medical supervision, they may work in other less well-supervised industries and are encouraged to conceal their pulmonary handicap. Wherever employed, they should be watched carefully; and the sputum, if present during colds or at other times, should be examined.—*La mise au travail des tuberculeux pulmonaires, P. Caspers, F. De Clercq, J. Beerens, & R. Wilkin, Acta tuberc. belg., June, 1953, 44: 211.—(A. T. Laird)*

**BCG Versus Vole Bacillus Vaccine.**—Previous work with vole bacillus vaccine had shown a high evidence of chronic ulceration when doses similar to BCG were used. More recently, the multiple puncture method was used and a study was undertaken to compare the results of vaccination with BCG and vole bacillus. A suspension of BCG, 20 mg. per ml., was used as opposed to vole bacillus, 20 mg. per ml. The subjects were medical students, nurses, and children, all of whom were tuberculin negative. Altogether, 197 persons were vaccinated. No ulcerations were observed.

Only one person in each group failed to become tuberculin-positive after seven weeks. Although 70 per cent of the persons vaccinated with vole bacillus were positive to 10 units of OT compared with 45.24 per cent in the BCG group, there was no significant difference in the rate of conversion.—*Multiple puncture with BCG and vole bacillus vaccine, I. M. Hall & J. A. H. Wylie, Lancet, September 27, 1952, 2: 608.*—(*A. G. Cohen*)

**Dry Oral BCG Vaccine.**—Oral BCG vaccination has been reported to reduce tuberculosis mortality to one-third or one-fifth of that found in nontuberculous children. Repeated oral revaccination so as to produce a state of minimal tuberculin sensitivity has been most successful, especially in newborn infants who live in highly infectious environments. To determine whether a dry BCG vaccine could be used orally, 297 children were vaccinated recently. Of the 53 newborn infants and 244 children between the ages of five months and ten years, 173 were vaccinated orally and 124 intradermally. In 74 cases, fresh BCG was used and, in 233, a dry vaccine which was prepared by the Paris Pasteur Institute. A single oral dose of 150 mg. of dry or 100 mg. of fresh BCG was employed. Intradermally, 0.1 mg. of either vaccine was used. The results obtained with the oral dry vaccine were in all respects comparable to those with fresh oral vaccine or the intradermal vaccinations. The use of this oral dry BCG would greatly facilitate vaccination throughout the world.—*Contribution a l'étude de la réaction de réinfection et de la sensibilité a la tuberculine chéz des enfants vaccinés avec le BCG sec par voie digestive, L. Sayé, Presse méd., April, 1953, 61: 524.*—(*V. Leites*)

**BCG Local Reaction.**—The increasing use of BCG makes it imperative that physicians recognize the skin lesion which BCG inoculation produces. This need was emphasized by 3 instances in which surgeons excised the ulcer of BCG inoculation. As a rule, BCG inoculation produces transient local erythema. A new area of reddening with deeper induration appears six weeks later and develops into a papule. During the next two weeks this papule becomes necrotic and a small, solitary, superficial, blue-red ulcer develops. After several weeks to six months the small, ulcerated area becomes encrusted and slowly forms a blue scar which later becomes white. The skin ulceration following BCG inoculation implies that the desired conversion of the tuberculin reaction from negative to positive will take place. Histologically, it is impossible to differentiate BCG skin changes from tuberculosis of the skin caused by virulent tubercle bacilli. Excision of the skin ulcer following BCG inoculation is not recommended.—*Art und Form der BCG—Hautläsion, H. Wespi, Schweiz. med. Wchnschr., March 14, 1953, 83: 260.*—(*E. Dunner*)

**Occupation and Lung Cancer.**—The age-adjusted mortality rate for lung cancer increased in the United States from 2.7 per 100,000 population in 1930 to 11.0 in 1948. This rate among men in 1948 was nearly four times as high (17.5 per 100,000) as the female rate of 4.6. The disease accounts for 3.1 per cent of all deaths among men 45 to 64 years of age. A statistical survey is being made by the California State Department of Health comparing a group of persons admitted for lung cancer to nine different private and public California hospitals with a control group of like ages without cancer or chest disease. Preliminary analysis of data on 408 lung cancer cases and 408 controls confirms the association between excessive cigarette smoking and lung cancer. Of 59 occupations listed, 5 showed a larger number of cases in the cancer group than in the control group. An exposure common to these 5 was metal fumes and particles. They included welders, crane men, firemen, metal miners, drillers, and tool dressers.—*Occupational factors in lung cancer, L. Breslow, Pub. Health Rep., March, 1953, 68: 286.*—(*S. J. Hadley*)

**Histoplasmin Sensitivity.**—Skin tests with histoplasmin, blastomycin, and coccidioidin were performed on 295 patients in the Mississippi State Sanatorium for tuberculosis. Of

the group, 65 (22 per cent) reacted positively to histoplasmin. Among northern Mississippi residents, 31.5 per cent were positive; among southern, 12.8 per cent. Only 0.7 per cent were positive to blastomycin and 0.7 per cent to coccidioidin. Neither of the 2 patients positive for blastomycin reacted to histoplasmin. Both of the positive coccidioidin reactors were positive to histoplasmin and both have lived in the San Joaquin Valley in California. The rates for both sexes and both white and Negro were approximately the same.—*Histoplasmin sensitivity in Mississippi—a new boundary, R. M. O'Neal, Pub. Health Rep., July, 1953, 68: 714.*—*(S. J. Hadley)*

**Histoplasmin Sensitivity in Texas.**—From April to August, 1951, 441 children ranging from infancy to sixteen years old were tested simultaneously with 1:1,000 Old Tuberculin and 1:100 histoplasmin. Most of the patients lived in and around Dallas, Texas. The over-all incidence of positive histoplasmin skin tests was 7 per cent (31 cases); and, of positive tuberculin skin tests, 4.5 per cent (20 cases). There was a definite trend for an increased sensitivity to histoplasmin as the subjects became older. The pattern for tuberculin positivity was much less regular. No case of clinical histoplasmosis was encountered. Comparison of these results with those from children in St. Louis, Missouri, shows that the incidence of positive histoplasmin skin tests is three to four times higher in the latter group.—*Histoplasmin and tuberculin sensitivity in Texas infants and children, G. B. Forbes & C. C. Chang, Pub. Health Rep., March, 1953, 68: 320.*—*(S. J. Hadley)*